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Diastereoselective Addition of Allylzinc Bromide to Imines Derived from (*R*)-Phenylglycine Amide

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General. Reagents were purchased from Aldrich Chemical Company and were used without further purification. Crotyl bromide was purchased from Fluka. (*R*)-Phenylglycine amide was provided by DSM (Geleen, The Netherlands). Commercial grade THF was used. Zinc-wool was cut prior to use. NMR spectra were recorded on either a Varian VXR-300 spectrometer (300 MHz) or a Varian Gemini Spectrometer (200 MHz). Chemical shifts are denoted in ppm and were referenced to residual solvent. Melting points (uncorrected) were determined on a Mettler FP-2 melting point apparatus equipped with a Mettler FP-21 microscope. HPLC analysis was performed on a HP1100 equipped with a Chiralpak or Crownpak analytical column.

Typical procedure for the synthesis of (*R*)-phenylglycine amide-imines 2-11. To a suspension of (*R*)-phenylglycine amide (200 mmol, 30.0 g) in CH₂Cl₂ (200 mL) at ambient temperature was added benzaldehyde (200 mmol, 21.2 g, 20.3 mL). The reaction mixture was stirred overnight at room temperature. MgSO₄ (10 g) was added and the reaction mixture was filtered. Evaporation of the solvent yields **2** as a colorless solid, which was recrystallized once from acetone/hexane (colorless crystals, 84%). m.p. 138-139 °C. ¹H NMR (200MHz, CDCl₃): δ 8.31 (s, 1H), 7.80 (m, 2H), 7.25-7.51 (m, 10H), 7.03 (bs, 1H), 5.84 (bs, 1H), 4.99 (s, 1H). ¹³C NMR (50 MHz, CDCl₃): δ 160.79, 129.04, 126.25, 126.03, 125.45, 124.81, 74.50. Anal. Calcd for C₁₅H₁₄N₂O: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.53; H, 5.99; N, 11.78.

(3). To a suspension of (*R*)-phenylglycine amide (15.0 g, 100 mmol) in CHCl₃, was added piperonal (15.0 g, 100 mmol) and a catalytic amount of *p*-TolSO₃H (0.3 g). The mixture was refluxed for 2 hours. MgSO₄ was added and the mixture was filtered. The filtrate was evaporated and the residue was crystallized from Et₂O. (colorless powder, 85 %) m.p. 138-139 °C. ¹H NMR (200 MHz, CDCl₃) δ 8.17 (s, 1H), 7.26-7.49 (m, 6H), 7.11-7.16 (m, 1H), 7.00 (bs, 1H), 6.81-6.86 (m, 1H), 6.02 (s, 1H), 6.03 (s, 1H), 5.86 (bs, 1H), 4.94 (s, 1H). ¹³C-NMR (50 MHz, CDCl₃): δ 173.19, 160.79, 149.04, 146.56, 138.03, 128.78, 127.20, 126.39, 125.79, 123.94, 106.64, 104.97, 100.14, 75.24. Anal. Calcd for C₁₆H₁₄N₂O₃: C, 68.08; H, 5.00; N, 9.92. Found: C, 67.74; H, 5.07; N, 9.97.

(4). (pale yellow powder, 90%) m.p. 139-140 °C. ¹H NMR (200 MHz, DMSO-*d*₆) δ 9.5 (bs, 1H), 8.25 (s, 1H), 7.69 (d, *J* = 8.57 Hz, 2H), 7.20-7.38 (m, 5H), 6.80 (d, *J* = 8.55 Hz, 2H), 4.73 (s, 1H), 3.34 (bs, 2H). ¹³C NMR (50 MHz, DMSO-*d*₆): δ 183.25, 172.08, 163.12, 160.88, 159.24, 139.62, 129.28, 127.22, 126.30, 126.06, 114.40, 75.63. Anal. Calcd for C₁₅H₁₄N₂O₂: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.02; H, 5.53; N, 10.69.

(5). (colorless crystals, 87%) m.p. 140-141 °C. ¹H NMR (200MHz, CDCl₃): 8.73 (s, 1H), 7.59 (d, *J* = 3.17 Hz, 1H), 7.46-7.51 (m, 2H), 7.26-7.39 (m, 3H), 6.97-7.03 (m, 2H), 6.83-6.88 (m, 1H), 4.99 (s, 1H), 3.83 (s, 3H), 3.81 (s, 3H). ¹³C NMR (50 MHz, CDCl₃): δ 173.14, 152.29, 152.10, 138.11, 127.15, 126.30, 125.75, 122.88, 117.37, 111.16, 109.78, 75.89, 54.62, 54.35. Anal. Calcd for C₁₇H₁₈N₂O₃: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.44; H, 6.14; N, 9.26.

(6). (colorless crystals, 90%). m.p. 113-114 °C. ¹H NMR (200MHz, CDCl₃) δ 8.93 (d, *J* = 1.46 Hz, 1H), 8.66 (d, *J* = 3.17 Hz, 1H), 8.33 (s, 1H), 8.14 (m, 1H), 7.26-7.47 (m, 6H), 6.9 (bs, 1H), 6.4 (bs, 1H), 5.00 (s, 1H). ¹³C NMR (50 MHz, DMSO-*d*₆): δ 171.34, 159.42, 150.69, 148.99, 139.03, 134.13, 130.11, 127.31, 126.35, 122.78, 75.84. Anal. Calcd for C₁₄H₁₃N₃O: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.01; H, 5.54; N, 17.49.

(7). (colorless crystals, 89 %) m.p. 144-145 °C. ¹H NMR (200MHz, CDCl₃): δ 8.07 (s, 1H), 7.26-7.56 (m, 6H), 7.04 (bs, 1H), 6.82-6.84 (m, 1H), 6.48-6.51 (m, 1H), 6.19 (bs, 1H), 4.92 (s, 1H). ¹³C NMR (50 MHz, CDCl₃): δ 169.88, 149.91, 149.57, 143.99, 137.67, 127.28, 126.52, 125.96, 114.45, 110.49, 75.64. Anal. Calcd for C₁₃H₁₂N₂O₂: C, 68.41; H, 5.30; N, 12.27. Found: C, 67.48; H, 5.29; N, 12.32.

(8). (pale yellow crystals, 80 %) m.p. 135-136 °C. ¹H NMR (200MHz, CDCl₃): δ 8.37 (s, 1H), 7.28-7.49 (m, 7H), 7.07-7.11 (m, 1H), 7.02 (bs, 1H), 5.63 (bs, 1H), 4.96 (s, 1H). ¹³C NMR (50MHz,CDCl₃):δ 172.81, 154.71, 140.12, 137.69, 130.53, 128.5, 127.24, 126.47, 126.19, 125.87, 74.72. Anal. Calcd for C₁₃H₁₂N₂OS: C, 63.91; H, 4.95; N, 11.47. Found: C, 63.76; H, 4.97; N, 11.30.

(9). (pale yellow plates, 95%) ^1H -NMR (300MHz, CDCl_3) δ 7.55 (s, 1H), 7.34 (d, 2H), 7.21-7.30 (m, 3H), 6.90 (bs, 1H), 5.90 (bs, 1H), 4.66 (s, 1H), 1.05 (s, 9H). ^{13}C -NMR (50MHz, CDCl_3) δ 174.77, 174.49, 139.41, 128.53, 127.67, 126.88, 76.33, 26.64. MS (CI): m/z =219 (M+1).

(10). (colorless crystals, 95%) m.p. 91-92 °C. ^1H NMR (200MHz, CDCl_3): δ 7.60 (d, J = 4.39, 1H), 7.21-7.37 (m, 5H), 6.90 (bs, 1H), 5.86 (bs, 1H), 4.67 (s, 1H), 2.46 (m, 1H), 1.06 (m, 6H). ^{13}C NMR (50 MHz, CDCl_3): δ 173.36, 170.92, 137.93, 127.09, 126.23, 125.58, 75.23, 32.71, 17.43, 17.37. Anal. Calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}$: C, 70.56; H, 7.89; N, 13.71. Found: C, 70.07; H, 7.85; N, 13.62.

(11). (colorless powder, 86%) m.p. 84-85 °C. ^1H NMR (200 MHz, CDCl_3) δ 7.74 (t, J = 5.1 Hz, 1H), 7.26-7.43 (m, 5H), 6.90 (bs, 1H), 5.68 (bs, 1H), 4.74 (s, 1H), 2.21 (m, 2H), 1.99 (m, 1H), 0.94 (m, 6H). ^{13}C -NMR (50 MHz, CDCl_3): δ 165.34, 126.14, 125.28, 124.63, 74.82, 42.44, 23.55, 20.03. Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.16; H, 8.25; N, 12.98.

Typical procedure for the allylation of (*R*)-phenylglycine amide-imines. A solution of allylzinc bromide (1.5 eq) was prepared by adding allylbromide (438 mmol, 38.5 mL) to finely cut zinc-wool (438 mmol, 28.6 g) in THF (250 mL). The solution of allylzinc bromide was cooled to room temperature and was added dropwise to a solution of **2** (292 mmol, 70 g) in THF (150 mL) at 0°C. The reaction mixture was warmed to room temperature and was poured into water (500 mL). EtOAc (200 mL) was added and the mixture was stirred vigorously. After filtration through a glass filter, the organic phase was separated and the water layer was extracted with EtOAc (2 x 100 mL). The combined organic layers were dried on MgSO_4 and concentrated to give **12** as a colorless oil that crystallized on standing (colorless crystals, 93%). m.p. 89-90 °C. ^1H NMR (200MHz, CDCl_3): δ 7.15-7.31 (m, 10H), 7.05 (bs, 1H), 6.22 (bs, 1H), 5.67-5.78 (m, 1H), 5.01-5.09 (m, 2H), 3.95 (s, 1H), 3.68 (t, J = 7.0 Hz, 1H), 2.40 (dd, J = 7.0 Hz, 2H). ^{13}C NMR (50 MHz, CDCl_3): δ 173.57, 140.33, 137.05, 132.60, 126.33, 126.14, 125.56, 124.97, 124.80, 124.59, 115.32, 61.91, 59.12, 40.16. Anal. Calcd for

$\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}$: C, 77.11; H, 7.19; N, 9.99. Found: C, 76.95; H, 7.22; N, 9.92.

(13). (colorless crystals, 81 %) m.p. 110-111 °C. ^1H NMR (200 MHz, CDCl_3) δ 7.21-7.23 (m, 5H), 6.93 (bs, 1H), 6.61-6.72 (m, 3H), 5.90 (s, 2H), 5.64-5.74 (bm, 2H), 5.00-5.07 (m, 2H), 3.99 (s, 1H), 3.60 (t, J = 6.96 Hz, 1H), 2.34-2.39 (dd, J = 6.96 Hz, 2H). ^{13}C NMR (50 MHz, CDCl_3) δ 174.24, 146.46, 145.30, 137.87, 135.21, 133.47, 127.31, 126.56, 125.72, 119.03, 116.25, 106.64, 105.47, 99.51, 59.92, 41.12. Anal. Calcd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_3$: C, 70.35; H, 6.21; N, 8.64. Found: C, 70.28; H, 6.33; N, 8.59.

(14). (colorless solid, 90%) m.p. 158-159 °C. ^1H NMR (200 MHz, $\text{DMSO}-d_6$) δ 9.20 (bs, 1H), 7.54 (s, 1H), 7.22-7.29 (m, 5H), 7.10 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 8.4 Hz, 2H), 5.70 (m, 1H), 5.00 (m, 2H), 3.87 (s, 1H), 3.50 (m, 1H), 2.25 (m, 2H). ^{13}C NMR (50 MHz, $\text{DMSO}-d_6$) δ 173.2, 155.2, 139.4, 134.8, 132.6, 127.2, 127.0, 125.9, 115.9, 113.9, 61.5, 58.7, 41.9. Anal. Calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.90; H, 6.84; N, 9.45.

(15). (yellow crystals, 93%) m.p. 121-122 °C. ^1H NMR (200MHz, CDCl_3): δ 7.48 (bs, 1H), 7.12-7.23 (m, 5H), 5.73-5.85 (m, 2H), 4.99-5.07 (m, 2H), 3.95 (s, 1H), 3.85 (t, J = 6.96 Hz, 1H), 3.86 (s, 3H), 3.60 (s, 3H), 2.40-2.45 (dd, J = 6.96 Hz, 2H). ^{13}C NMR (50 MHz, CDCl_3): δ 198.91, 174.71, 152.02, 150.14, 138.30, 134.39, 129.75, 127.21, 126.40, 125.75, 115.72, 113.14, 110.91, 110.28, 63.36, 57.30, 54.15, 54.05, 39.02. Anal. Calcd for $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_3$: C, 70.57; H, 7.11; N, 8.23. Found: C, 70.38; H, 7.16; N, 8.13.

(16). (pale yellow powder, 43 %). m.p. 96-97 °C. ^1H NMR (200MHz, CDCl_3) δ 8.58 (s, 2H), 7.77 (d, J = 7.69 Hz, 1H), 7.36 (m, 1H), 7.15 (m, 5H), 6.41 (bs, 1H), 5.45-5.65 (m, 2H), 5.00 (m, 2H), 3.89 (s, 1H), 3.79 (t, J = 7.04 Hz, 1H), 2.38 (m, 2H). ^{13}C NMR (50 MHz, $\text{DMSO}-d_6$): δ 172.91, 147.64, 147.00, 138.99, 138.34, 134.94, 133.81, 127.06, 125.92, 122.97, 116.72, 61.72, 56.97, 41.27. Calcd for $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}$: C, 72.57; H, 6.81; N, 14.93. Found: C, 72.50; H, 6.81; N, 15.1.

(17). (colorless solid, 88 %) m.p. 77-78 °C. ^1H NMR (200MHz, CDCl_3) δ 7.21-7.35 (m, 6H), 6.30-6.33 (m, 1H), 6.17-6.19 (m, 1H), 6.14 (bs, 1H), 5.69-5.90 (m, 1H), 5.07-5.17 (m, 2H), 4.11 (s, 1H), 3.74 (t, J = 6.84 Hz, 1H), 2.47-2.55 (m,

2H). ^{13}C NMR (50 MHz, CDCl_3): δ 174.56, 153.57, 140.38, 137.87, 133.08, 127.28, 126.56, 126.34, 125.87, 116.47, 108.55, 105.89, 63.09, 53.46, 37.99.

(18). (yellow crystals, 90%) m.p. 62-63 °C. ^1H NMR (200MHz, CDCl_3): δ 7.22-7.30 (m, 6H), 6.89-6.97 (bm, 3H), 5.75-5.89 (bm, 2H), 5.08-5.09 (m, 2H), 4.19 (s, 1H), 4.02 (t, J = 6.8 Hz, 1H), 2.50-2.58 (m, 2H). ^{13}C NMR (50 MHz, CDCl_3): δ 174.02, 145.95, 137.67, 132.99, 127.28, 126.56, 125.83, 125.03, 123.57, 122.82, 116.66, 62.75, 55.53, 41.63. Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}$: C, 67.10; H, 6.34; N, 9.78. Found: C, 66.95; H, 6.32; N, 9.73.

(19) (yellow oil, 89%) ^1H -NMR (300MHz, CDCl_3) δ 7.18-7.26 (m, 5H), 6.85 (bs, 1H), 6.77 (bs, 1H), 5.75-5.89 (m, 1H), 4.95-5.06 (m, 2H), 4.28 (s, 1H), 2.33-2.38 (m, 1H), 2.15-2.18 (m, 1H), 1.95-2.06 (m, 1H), 0.76 (s, 9H). ^{13}C -NMR (50MHz, CDCl_3) δ 176.24, 139.44, 137.76, 128.47, 127.80, 127.75, 65.89, 63.89, 36.09, 35.22, 26.91. MS (CI): m/z =261 (M+1).

(20). (yellowish oil, 77 %). ^1H NMR (200MHz, CDCl_3): δ 7.20-7.34 (m, 6H), 6.02 (bs, 1H), 5.76 (m, 1H), 5.07 (d, J = 10.6 Hz, 1H), 5.03 (s, 1H), 4.25 (s, 1H), 2.37 (m, 1H), 2.17 (m, 1H), 1.87 (m, 2H), 0.85 (d, J = 6.6 Hz, 3H), 0.72 (d, J = 6.9 Hz, 3H). ^{13}C NMR (50 MHz, CDCl_3): δ 174.02, 137.24, 134.00, 126.32, 125.54, 124.96, 114.74, 62.39, 58.53, 32.23, 26.79, 16.45, 14.53. Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}$: C, 73.13; H, 9.00; N, 11.37. Found: C, 73.13; H, 9.23; N, 11.16.

(21). (pale yellow solid, 94%) m.p. 56-57 °C. ^1H NMR (200 MHz, CDCl_3) δ 7.18-7.39 (m, 6H), 5.88 (bm, 2H), 5.04-5.14 (m, 2H), 4.28 (s, 1H), 2.58 (m, 1H), 2.16 (m, 2H), 1.60 (m, 2H), 1.22 (m, 2H), 0.80 (m, 6H). ^{13}C NMR (50 MHz, CDCl_3) δ 174.9, 138.3, 133.79, 127.3, 126.5, 125.9, 116.1, 63.3, 52.14, 42.5, 37.4, 23.3, 21.3, 21.2. Anal. Calcd for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}$: C, 73.81; H, 9.29; N, 10.76. Found: C, 73.81; H, 9.43; N, 10.67.

(22). A solution of crotylzinc bromide (1.5 eq) was prepared by adding crotylbromide (62.6 mmol, 6.4 mL) to finely cut zinc-wool (62.6 mmol, 4.0 g) in THF (50 mL). The solution of crotylzinc bromide was cooled to room temperature and was added dropwise to a solution of **2** (41.7 mmol, 10 g) in THF (30 mL)

at 0°C. The reaction mixture was warmed to room temperature and was poured into water (100 mL). EtOAc (30 mL) was added and the mixture was stirred vigorously. After filtration through a glass filter, the organic phase was separated and the water layer was extracted with EtOAc (2 x 30 mL). The combined organic phase was dried over MgSO_4 and concentrated to give **22**. (orange oil, 98%). ^1H NMR (200 MHz, CDCl_3) δ 6.99-7.29 (m, 2x10H), 6.69 (bs, 1H), 6.44 (bs, 1H), 5.72-5.84 (m, 1H), 4.46-5.58 (m, 1H), 4.98-5.15 (m, 2x2H), 3.97 (s, 1H), 3.89 (s, 1H), 3.70 (d, J = 5.13 Hz, 1H), 3.36 (d, J = 8.42 Hz, 1H), 2.41-2.65 (m, 1H), 2.31-2.41 (m, 1H), 0.92 (d, J = 6.95 Hz, 3H), 0.78 (d, J = 6.59 Hz, 3H). ^{13}C NMR (50 MHz, CDCl_3) δ 175.5, 175.2, 139.9, 139.7, 138.0, 137.5, 136.9, 127.6, 127.3, 127.0, 126.8, 126.7, 126.7, 126.3, 126.2, 126.1, 125.8, 115.3, 114.6, 65.3, 64.9, 62.6, 62.5, 43.2, 42.2, 16.3, 15.0.

(23). A solution of methallylzinc bromide (1.5 eq) was prepared by adding methallylbromide (62.6 mmol, 6.3 mL) to finely cut zinc-wool (62.6 mmol, 4.0 g) in THF (50 mL). The solution of methallylzinc bromide was cooled to room temperature and was added dropwise to a solution of **2** (41.7 mmol, 10 g) in THF (30 mL) at 0°C. The reaction mixture was warmed to room temperature and was poured into water (100 mL). EtOAc (30 mL) was added and the mixture was stirred vigorously. After filtration through a glass filter, the organic phase was separated and the water layer was extracted with EtOAc (2 x 30 mL). The combined organic layers were dried over MgSO_4 and concentrated to give **23** that can be crystallized from Et_2O (colorless solid, 98%). m.p. 104-109 °C. ^1H NMR (200 MHz, CDCl_3) δ 7.14-7.30 (m, 10H), 6.95 (bs, 1H), 5.76 (bs, 1H), 4.80 (s, 1H), 4.73 (s, 1H), 4.00 (s, 1H), 3.75-3.80 (m, 1H), 2.27-2.43 (m, 2H), 1.72 (s, 3H). ^{13}C NMR (50 MHz, CDCl_3) δ 175.1, 140.7, 140.5, 136.9, 127.4, 127.2, 126.8, 126.2, 125.9, 125.7, 112.4, 63.7, 62.5, 44.9, 21.1.

Typical procedure for the catalytic hydrogenation of (*R*)-phenylglycine amide-homoallylamines. Homoallylamine **12** (15.0 mmol, 4.2 g) was dissolved in MeOH (100 mL). Water (10 mL), acetic acid (2.5 mL), and Pd(10%)/C (0.6 gram) were added successively. The mixture was shaken under an atmosphere of H_2 (30 psi) for 18 hrs at room temperature. The MeOH was evaporated under reduced pressure. The residue was diluted with water (50 mL) and

was adjusted to pH = 10 with 10 % NaOH. The water phase was extracted with CH₂Cl₂ (3 x 40 mL). The combined organic phase was dried on MgSO₄ and filtered. After evaporation of the CH₂Cl₂, pentane was added to the residue. Filtration through a glass filter yields crystalline phenylacetamide (0.8 g, 41%). Evaporation of the pentane left (*R*)-**24** as a colorless oil that slowly solidified on standing (1.1 g, 49%). [α]_D²⁷₅₈₉ +18.3 (*c* = 1.06, CHCl₃). ¹H NMR (200MHz, CDCl₃): δ 7.20-7.34 (m, 5H), 3.89 (t, *J* = 6.84 Hz, 1H), 1.97 (bs, 2H), 1.60-1.69 (m, 2H), 1.21-1.36 (m, 2H), 0.93 (t, *J* = 7.08 Hz, 3H). ¹³C NMR (50 MHz, CDCl₃): δ 141.21, 126.95, 125.81, 125.33, 53.85, 37.93, 17.81, 12.41.

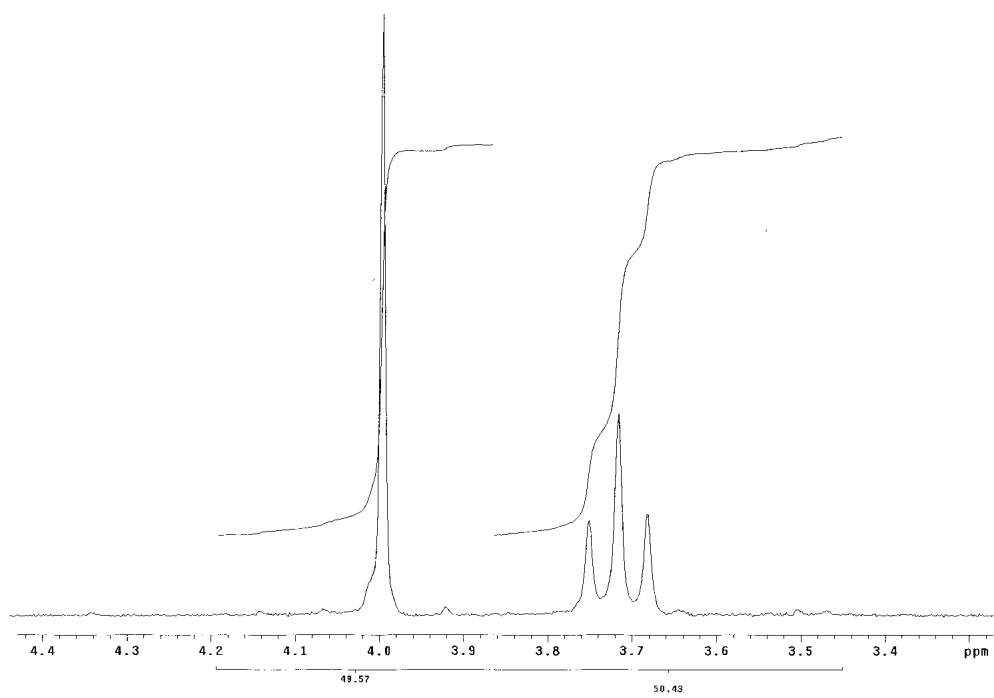
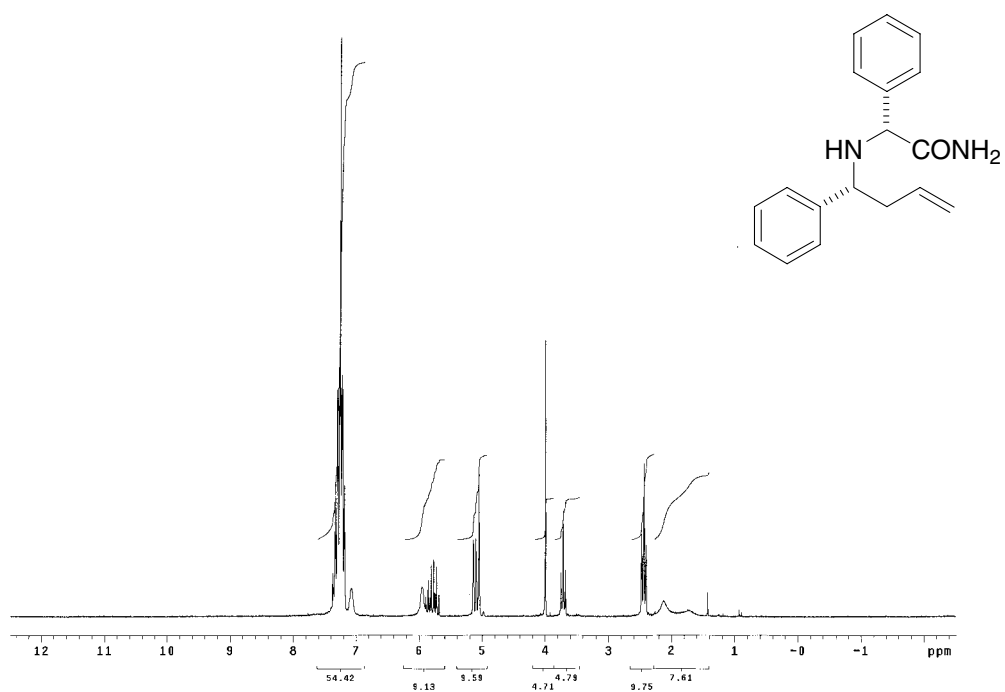
(*R*)-**25** (colorless oil, 64%). [α]_D²⁷₅₈₉ +17.0 (*c* = 0.99, CHCl₃). ¹H NMR (200MHz, CDCl₃): δ 2.38-2.44 (m, 1H), 0.85-1.40 (m, 8H), 0.74-0.84 (m, 9H). ¹³C NMR (50 MHz, CDCl₃): δ 54.5, 35.4, 31.6, 18.0, 17.5, 15.3, 12.5.

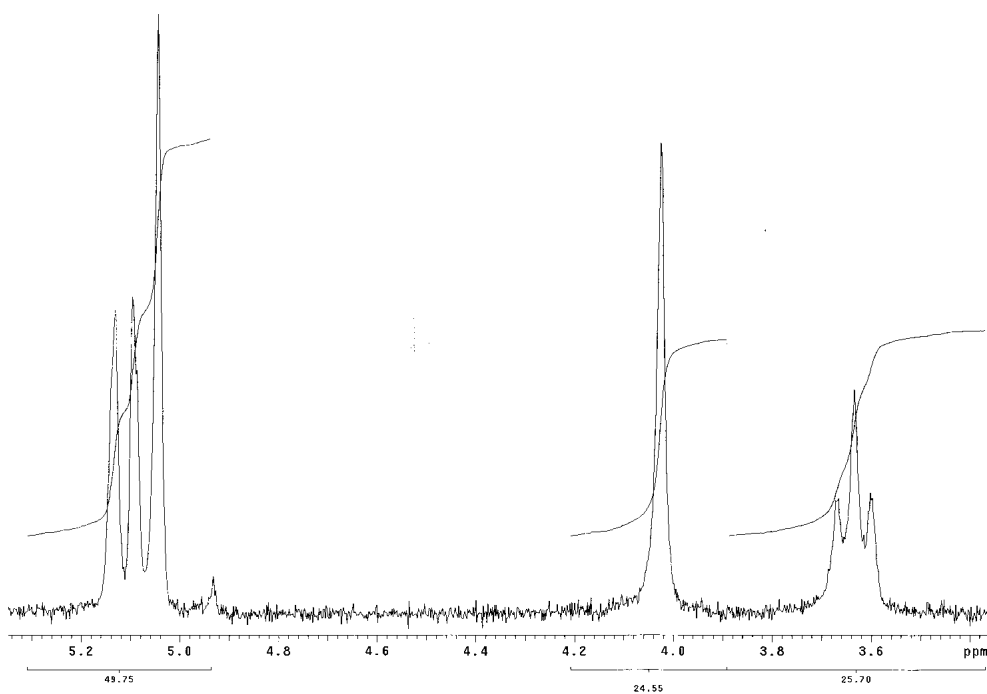
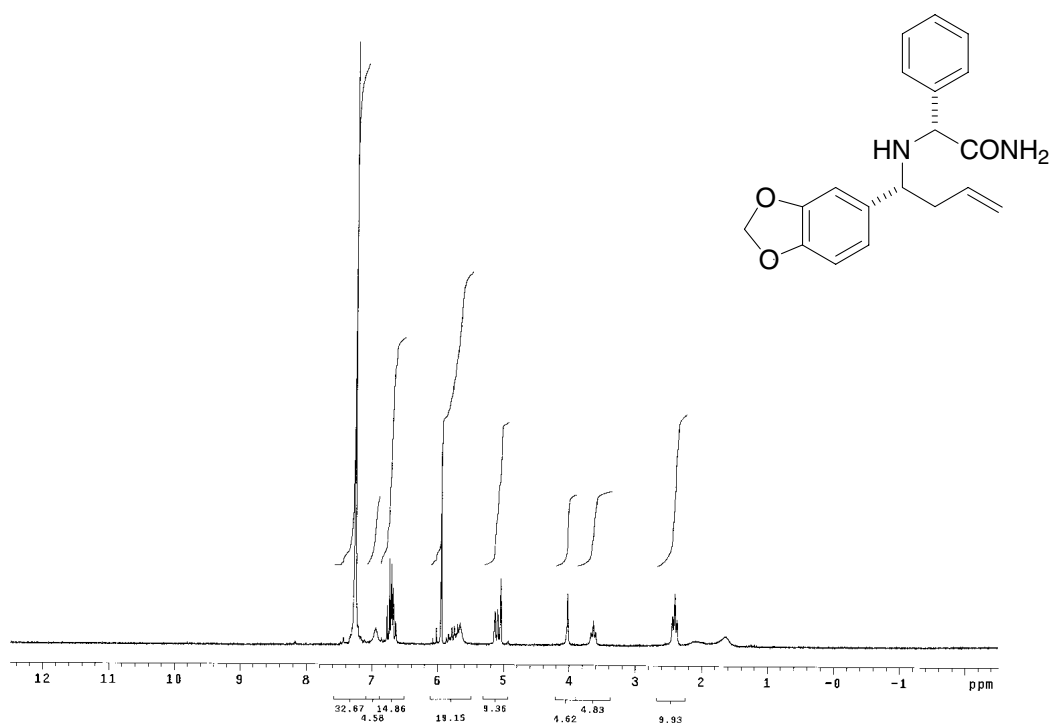
(*R*)-**26** (colorless oil, 88 %). [α]_D²⁷₅₈₉ +10.9 (*c* = 1.01, CHCl₃). ¹H NMR (200MHz, CDCl₃): δ 6.83 (s, 1H), 6.74 (s, 2H), 5.92 (s, 2H), 3.80 (bs, 1H), 1.58-1.63 (bm, 2H), 1.18-1.26 (bm, 2H), 0.89 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (50 MHz, CDCl₃): δ 146.08, 144.67, 139.35, 117.85, 106.32, 105.00, 99.22, 54.22, 40.30, 18.15, 12.44.

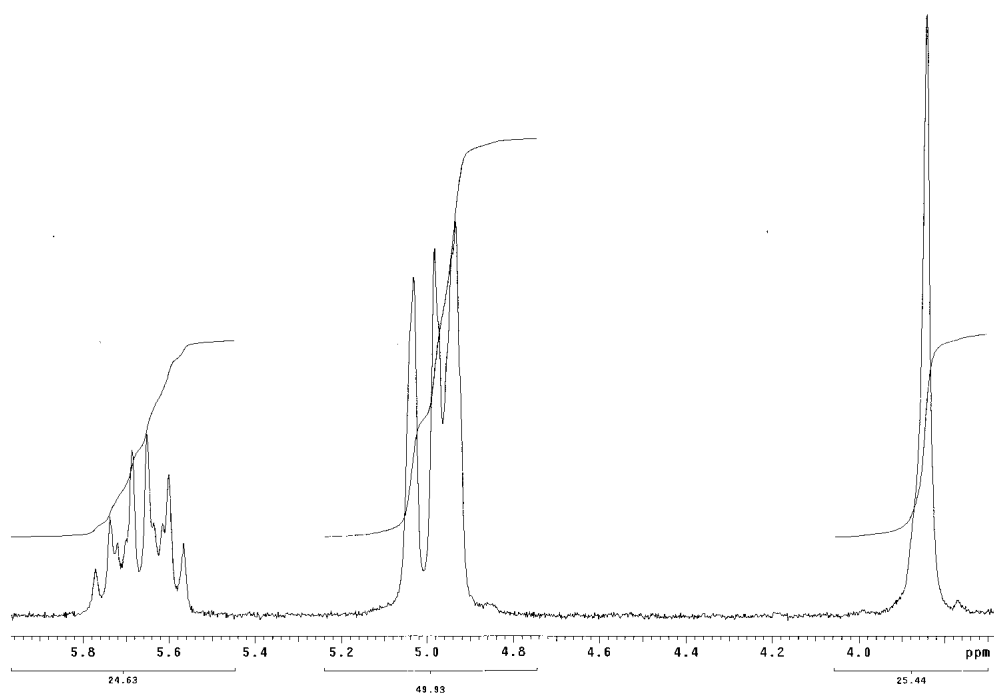
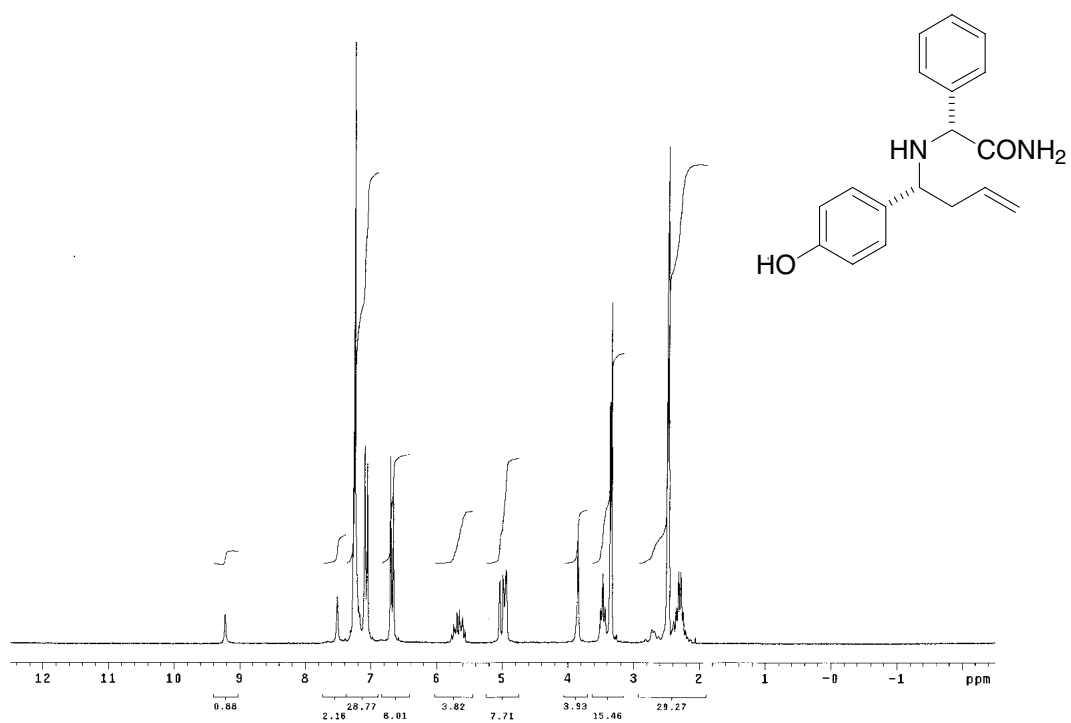
Typical procedure for the non-reductive auxiliary removal (retro-Strecker method). To CH₂Cl₂ (600 mL), cooled with an ice bath, was added DMF (144 mmol, 10.6 g, 11.2 mL). Oxalylchloride (144 mmol, 18.5 g, 12.7 mL) was added dropwise. After the formation of gas (CO and CO₂) had ceased, a solution of amide **20** (97.6 mmol, 24.0 g) in CH₂Cl₂ (100 mL) was added dropwise in 10 minutes. Triethylamine (97.5 mmol, 9.8 g, 13.48 mL) was added dropwise in 5 minutes turning the reaction mixture orange-red. The reaction was stirred at room temperature for 30 minutes. Water (300 mL) was added and the organic phase was separated. The aqueous layer was washed with CH₂Cl₂ (100 mL) additionally. The organic layer was dried over Na₂SO₄ and concentrated to give the crude nitrile **28** (22.0 g, 95.6 mmol, 98%) as an orange oil. The crude nitrile (7.4 g; 33 mmol) was dissolved in ethanol (150 mL) and K₂CO₃ (8.97 g; 65 mmol; 2 eq.) was added. The reaction mixture was refluxed for 2 hours. The ethanol was evaporated and the residue was taken up in

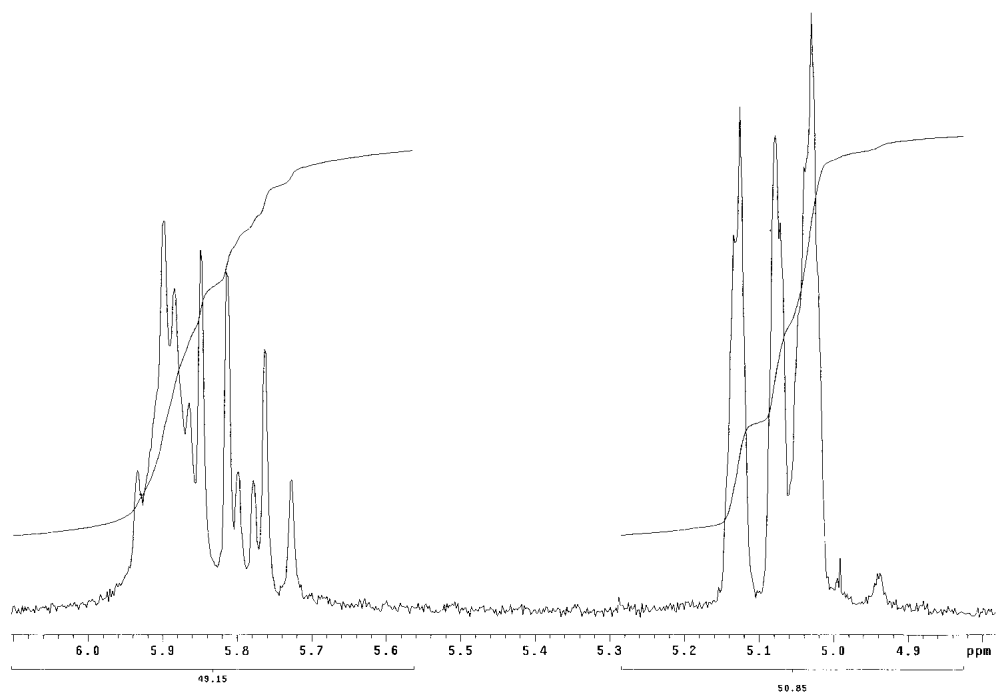
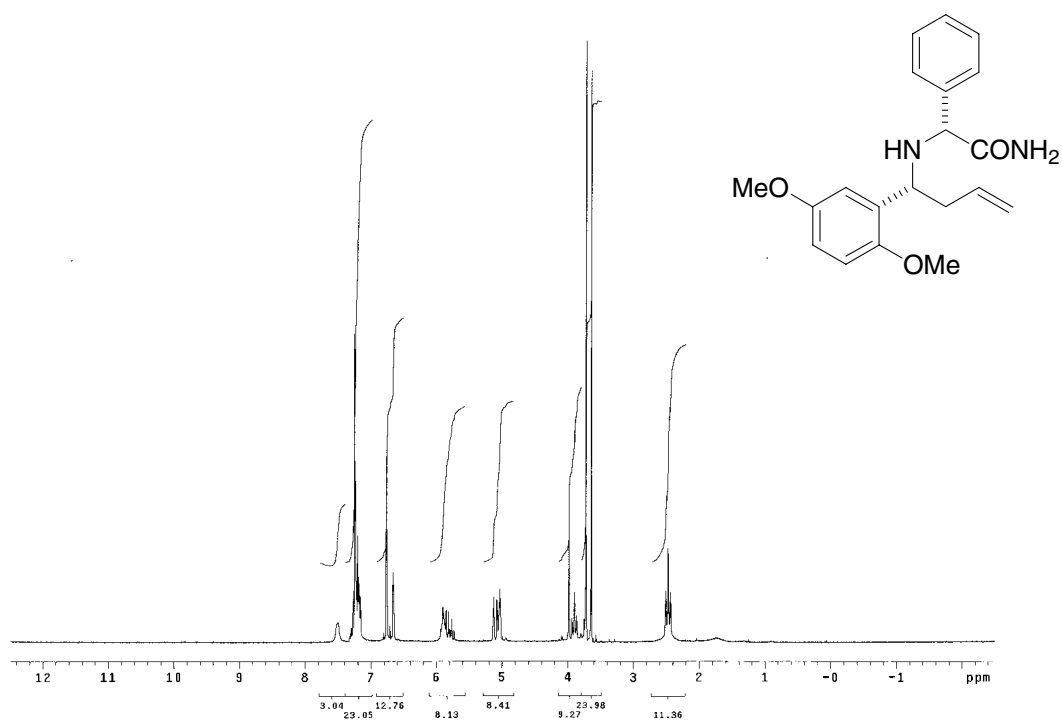
water/CH₂Cl₂. The organic phase was separated and dried over Na₂SO₄. Evaporation of the solvent gives the crude imine **30** (6.2 g, 30.8 mmol, 93%) as the only product. ¹H NMR (200MHz, CDCl₃): δ 8.11 (s, 1H), 7.68-7.71 (m, 2H), 7.27-7.37 (m, 3H), 5.61-5.70 (m, 1H), 4.91-4.99 (m, 2H), 2.81-2.87 (m, 1H), 2.33-2.41 (m, 2H), 1.82-1.89 (m, 1H), 0.86-0.91 (m, 6H). ¹³C NMR (50 MHz, CDCl₃): δ 157.99, 135.01, 134.90, 128.74, 126.96, 126.65, 114.87, 75.79, 36.55, 31.14, 18.32, 17.11. MS (EI) [*m/e*, %]: 201 [M⁺, 4.3]; 160 [M⁺-C₃H₅, 100]. Imine **30** (2.0 g, 9.94 mmol) was dissolved in a 50% aqueous THF. 3 equivalents of NH₂OH.HCl (2.08 g, 29.8 mmol) were added and the reaction mixture was stirred overnight at ambient temperature. The THF was evaporated under reduced pressure and the residue was treated with aqueous HCl (30 %) until pH = 1. The aqueous phase was extracted with EtOAc. The water phase was adjusted to pH = 10 with aqueous NaOH (33 %) and was extracted with CH₂Cl₂. After drying over Na₂SO₄, the solvent was evaporated furnishing the homoallylamine **32** (yellowish oil, 1.03 g, 9.14 mmol, 92 % (84 % overall from **20**), er 99/1). ¹H NMR (200MHz, CDCl₃): δ 5.61-5.83 (m, 1H), 5.02-5.12 (m, 2H), 2.53-2.60 (m, 1H), 2.20-2.26 (m, 1H), 1.87-2.01 (m, 1H), 1.58-1.62 (m, 1H), 0.86-0.92 (m, 6H). ¹³C NMR (50 MHz, CDCl₃): δ 134.61, 115.54, 54.23, 37.50, 31.18, 17.50, 15.99. [α]_D²⁷₅₈₉ -8.1 (*c* = 1.04, CHCl₃).

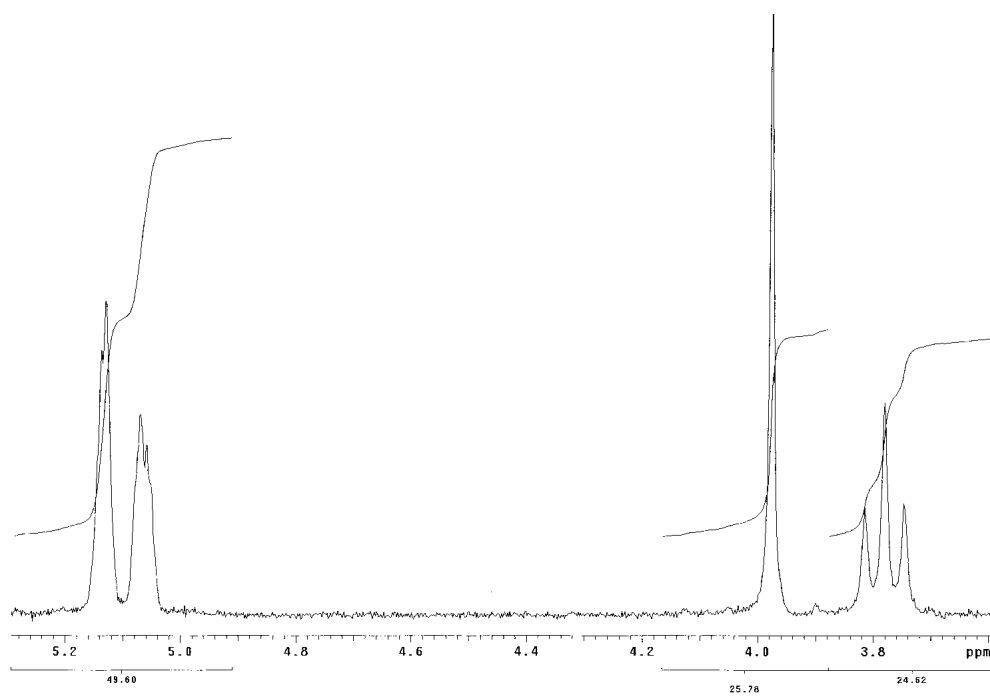
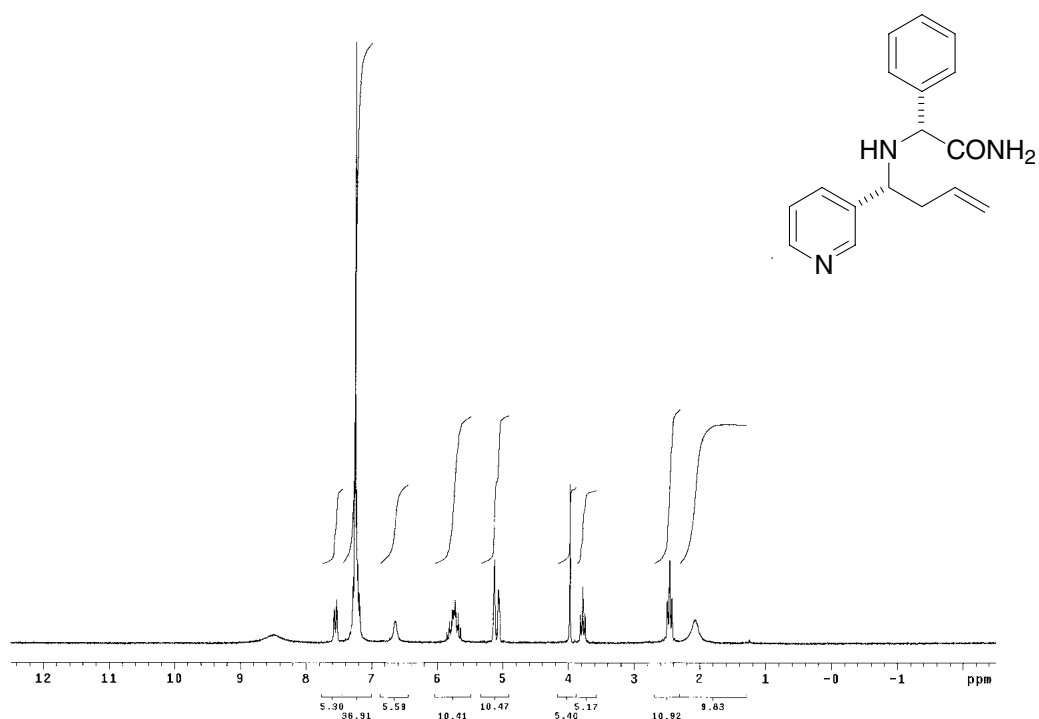
(**31**) (yellowish oil, 78% overall from **12**). ¹H NMR (200MHz, CDCl₃): δ 7.10-7.25 (m, 5H), 5.60-5.80 (m, 1H), 5.00-5.20 (m, 2H), 3.90-4.00 (m, 1H), 2.20-2.50 (m, 2H). ¹³C NMR (50 MHz, CDCl₃): δ 145.85, 135.49, 128.35, 126.91, 126.34, 117.50, 55.37, 44.19.



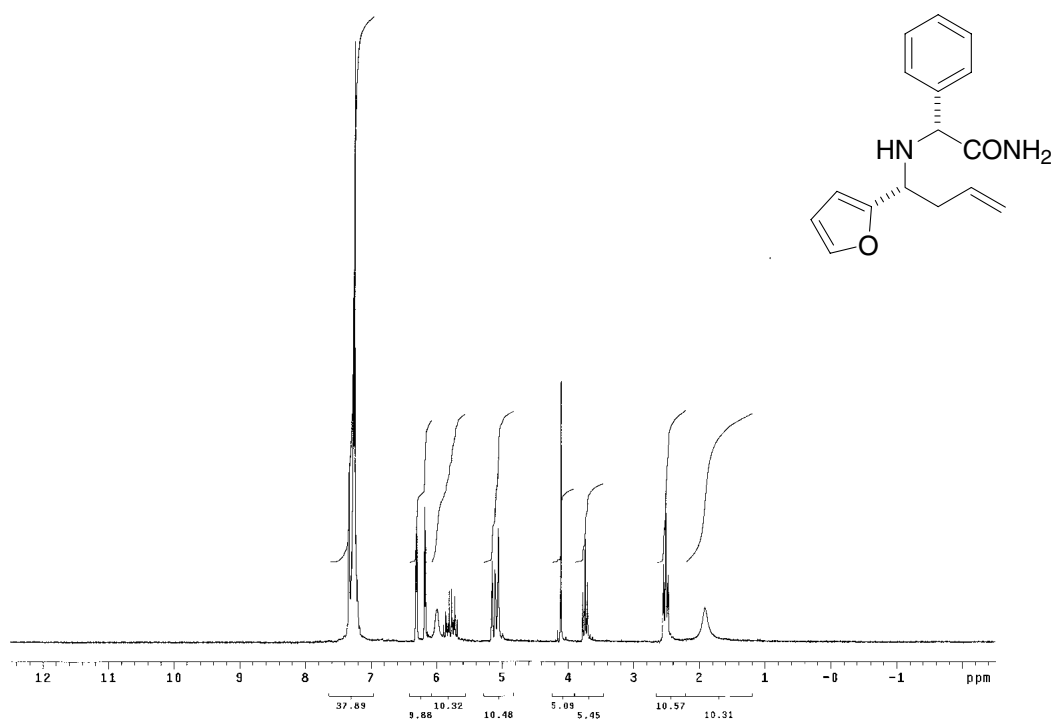




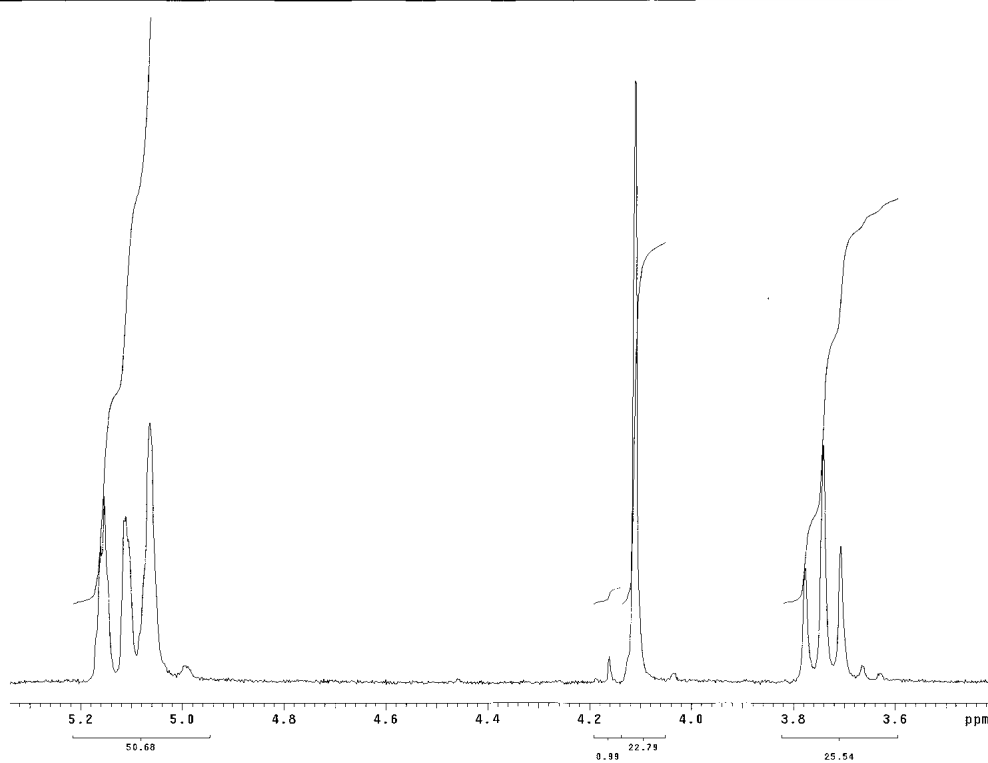


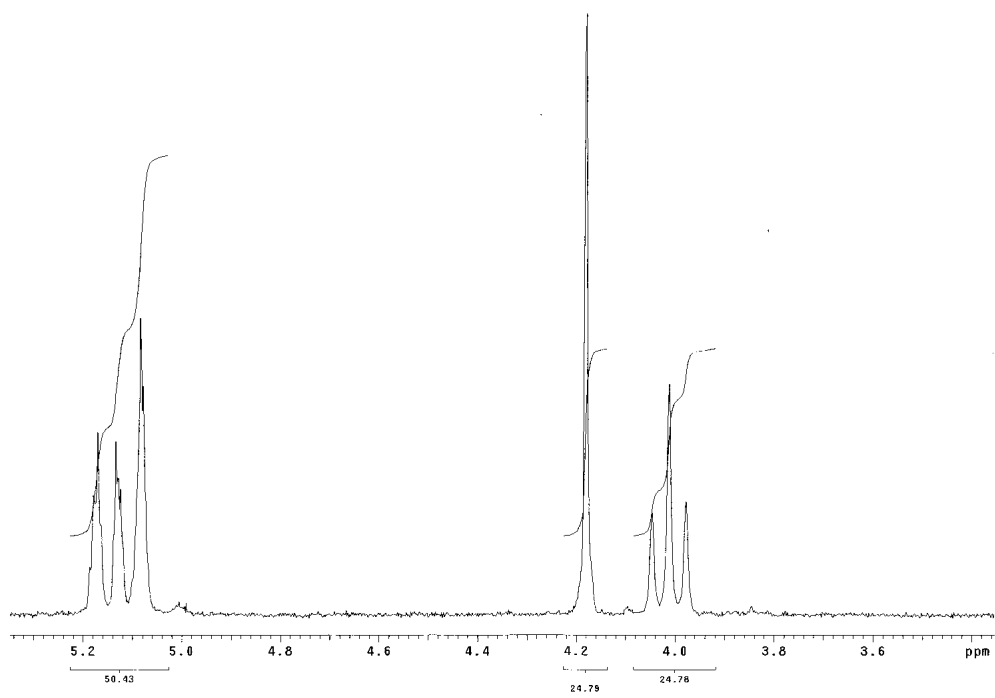
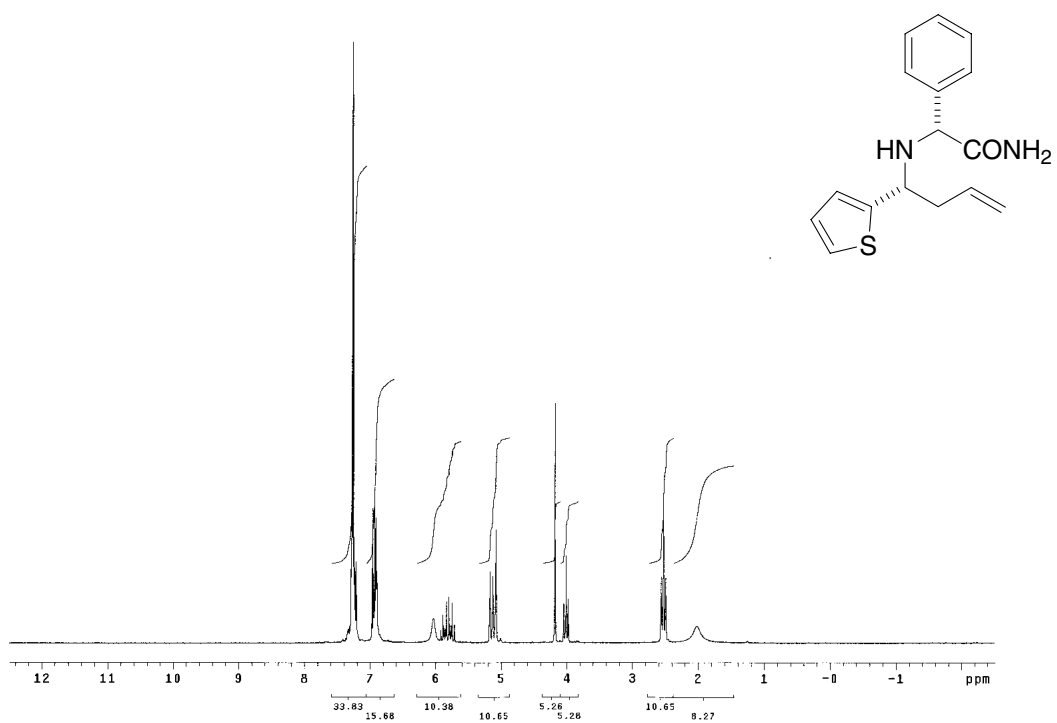


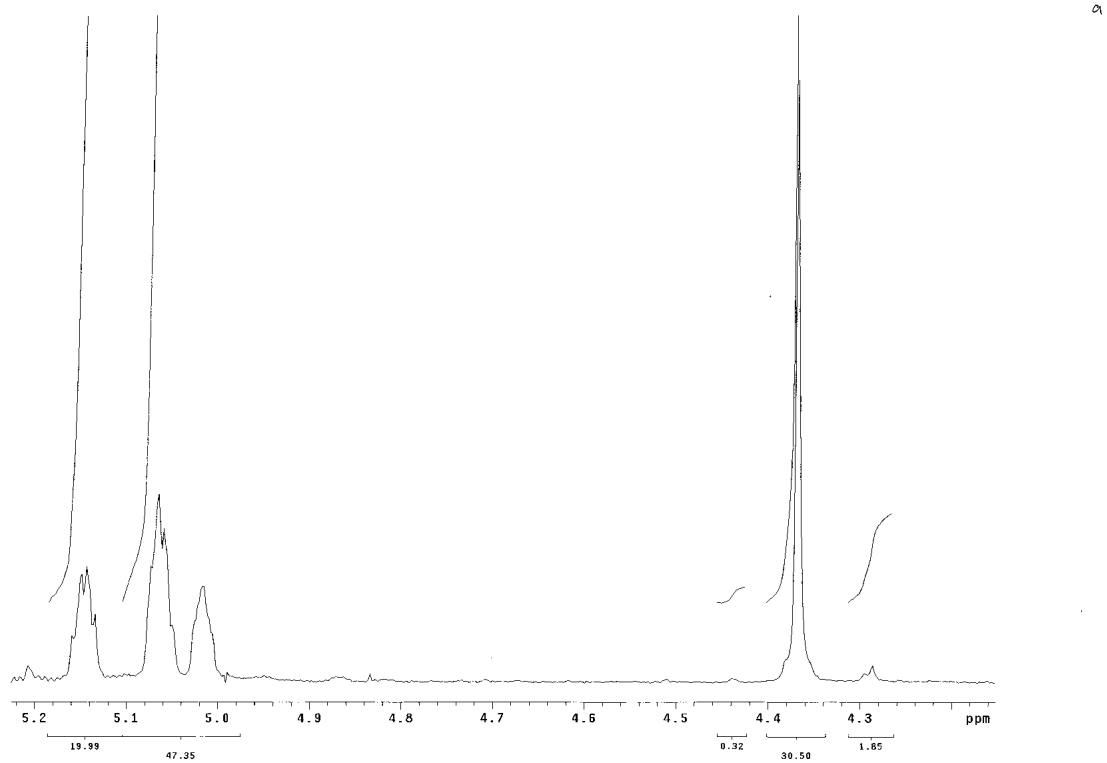
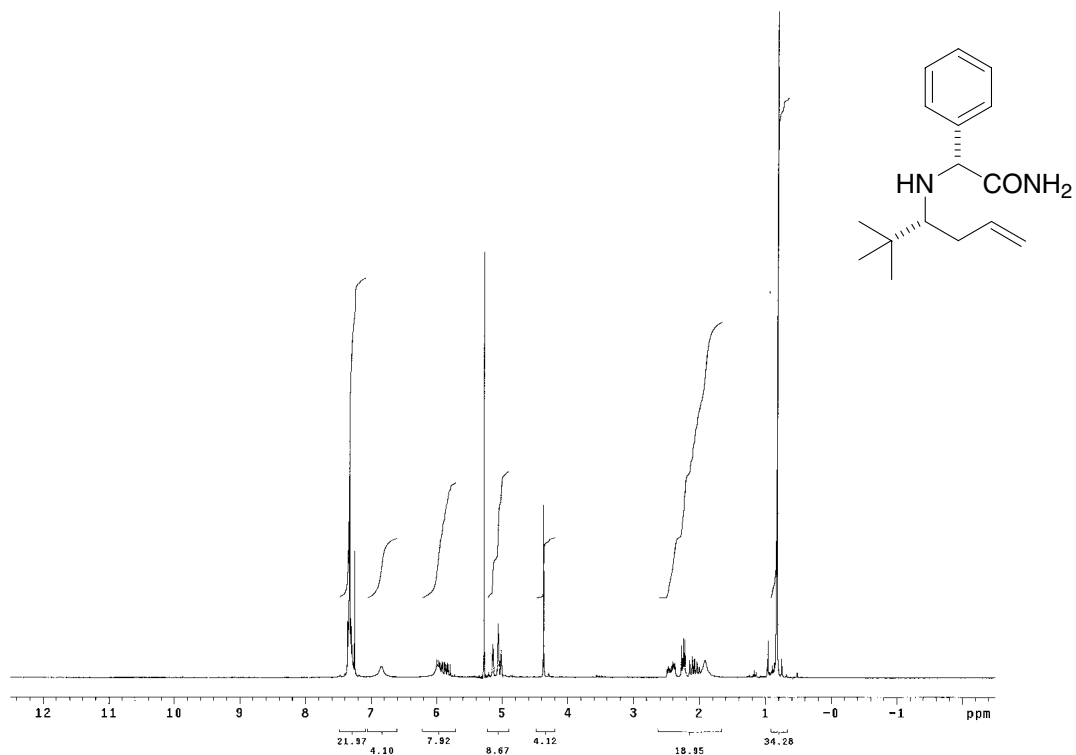
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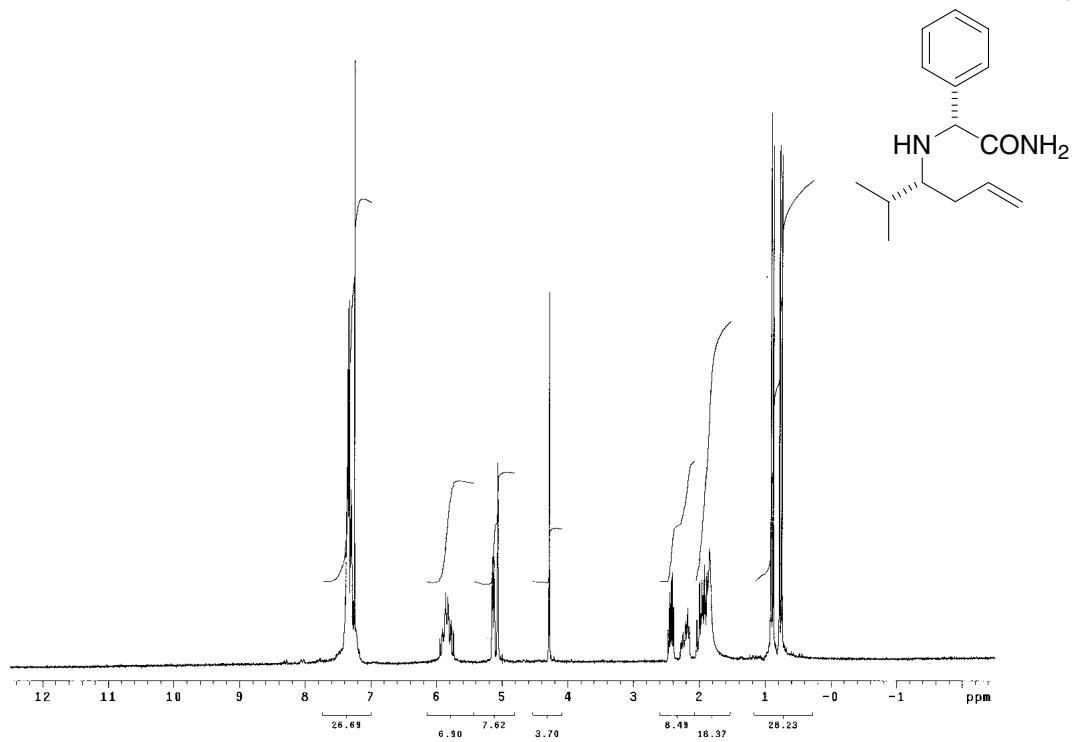
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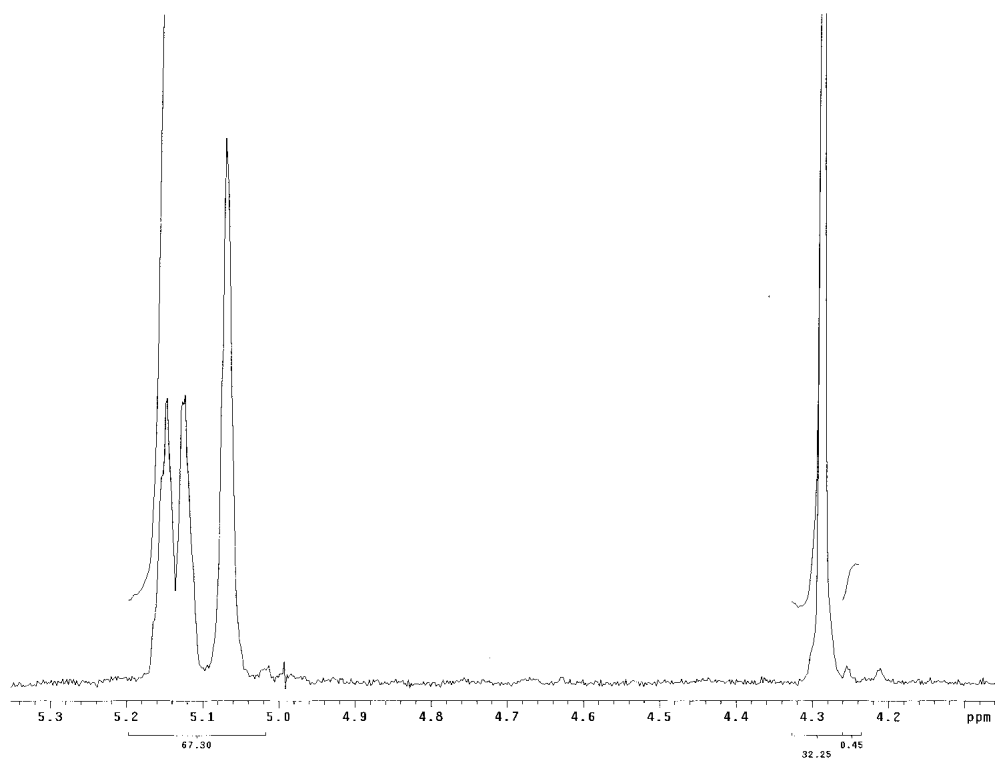


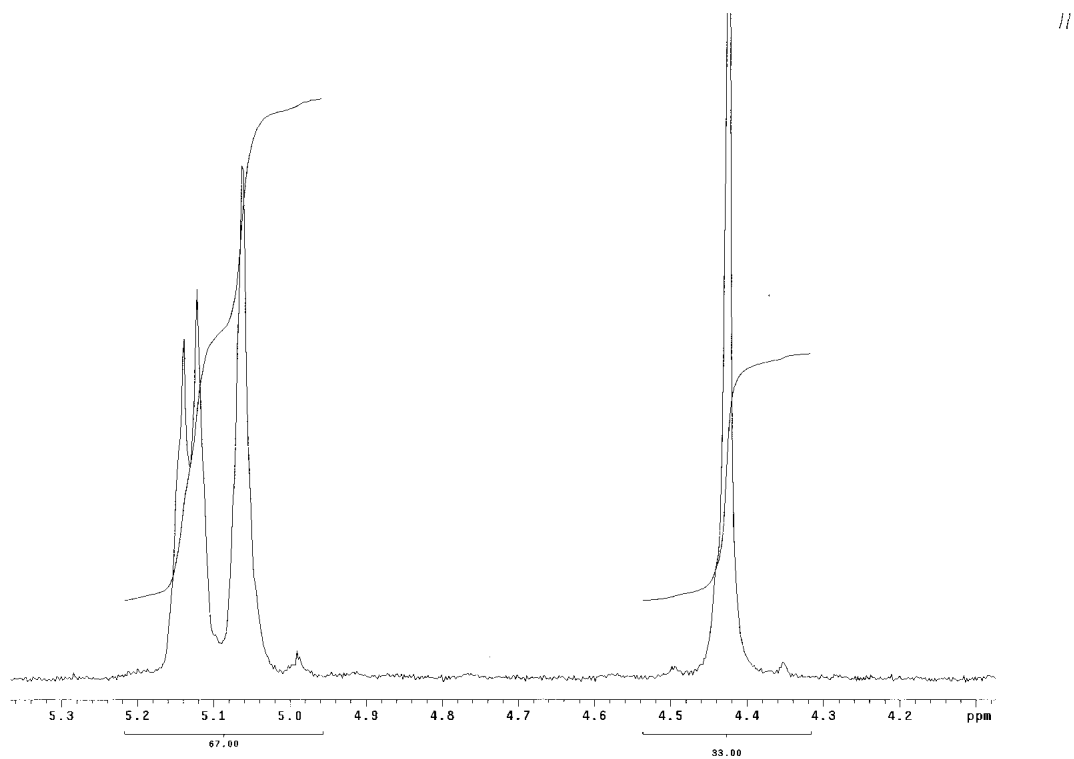
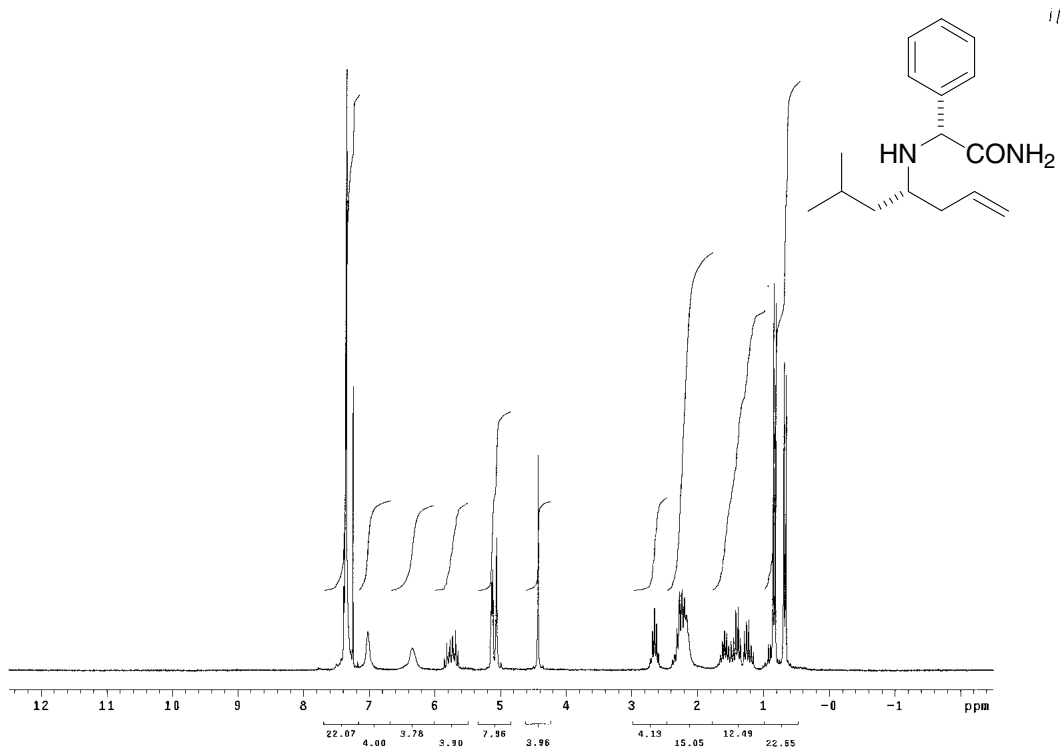


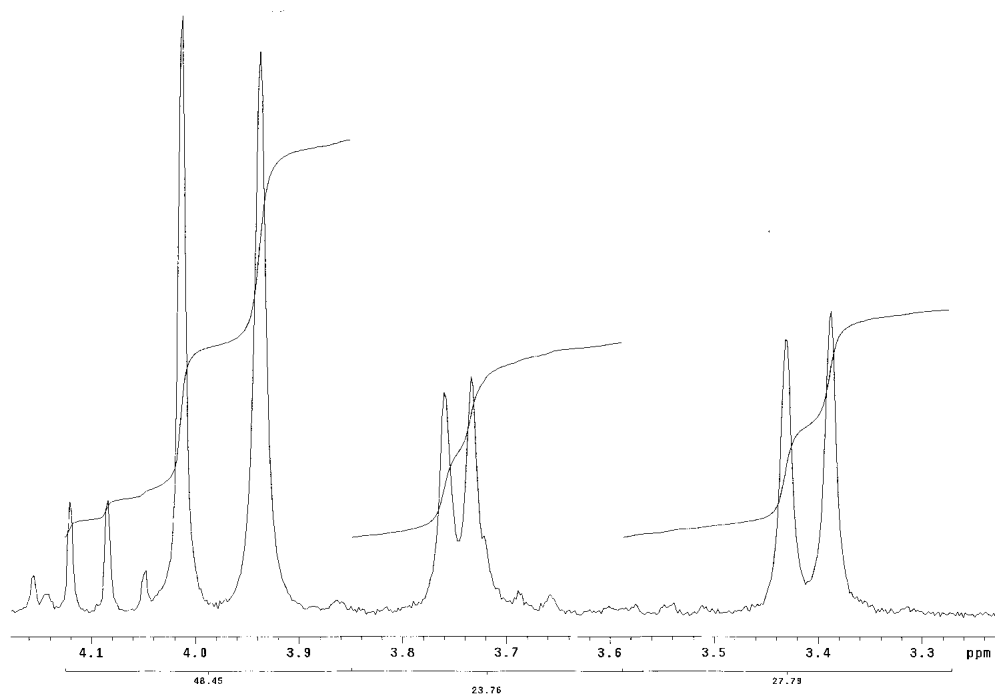
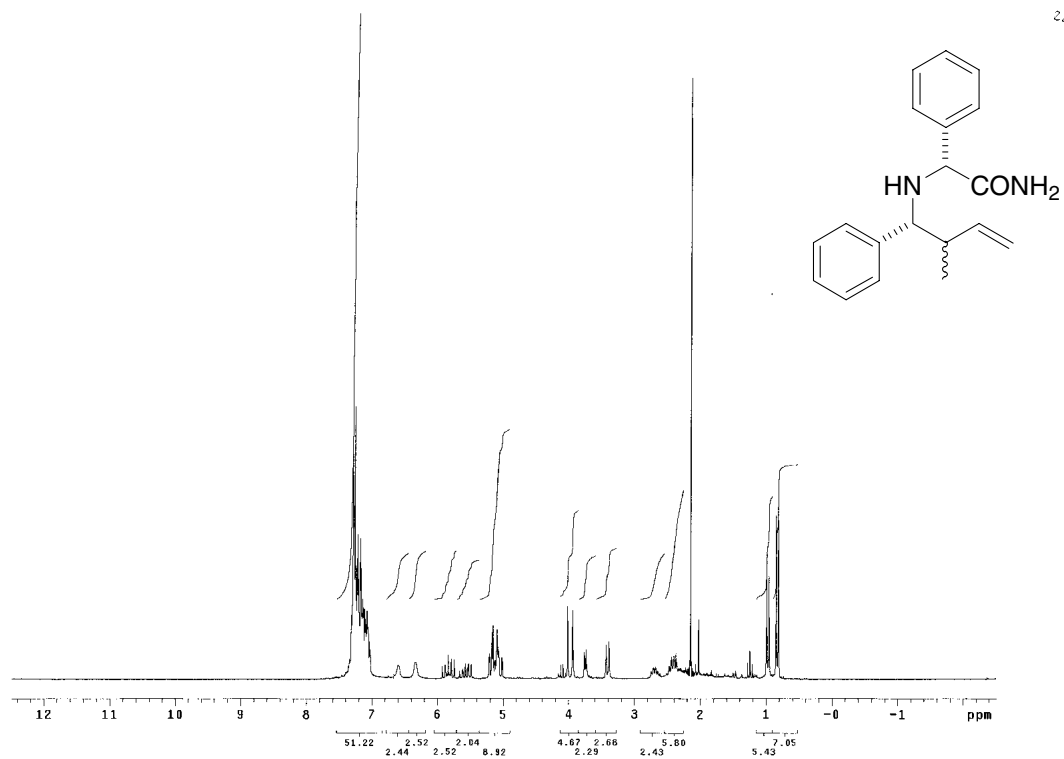
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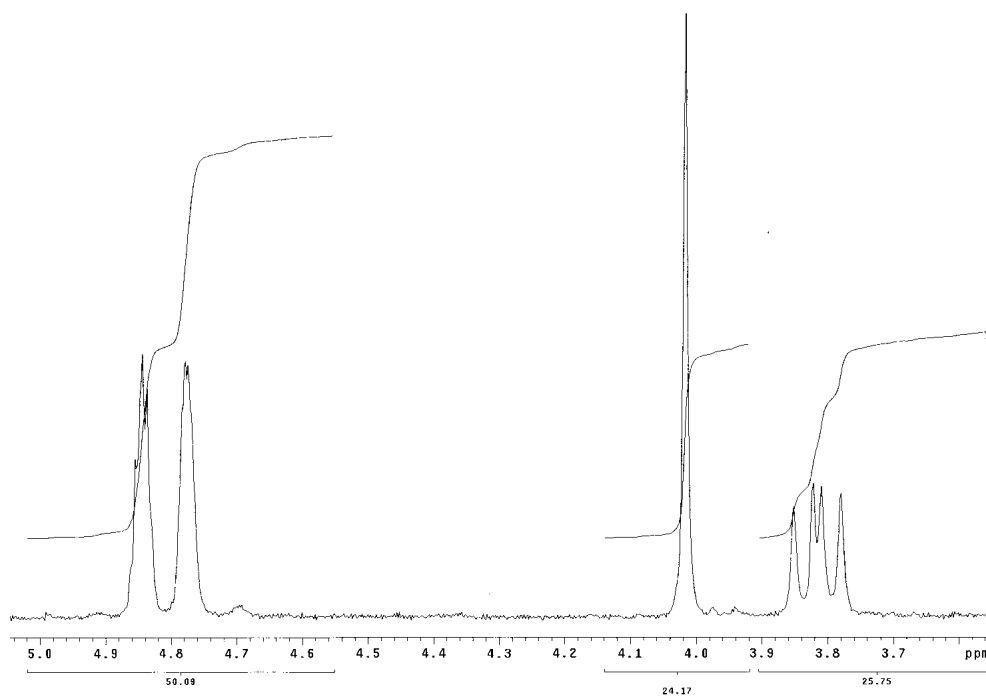
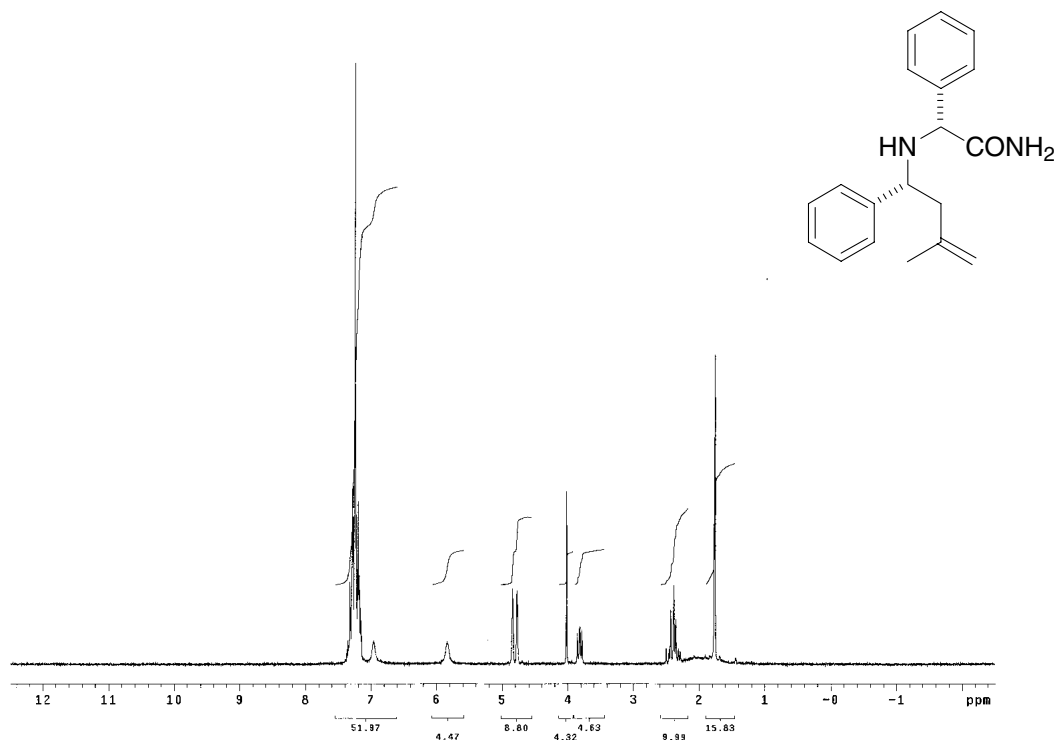


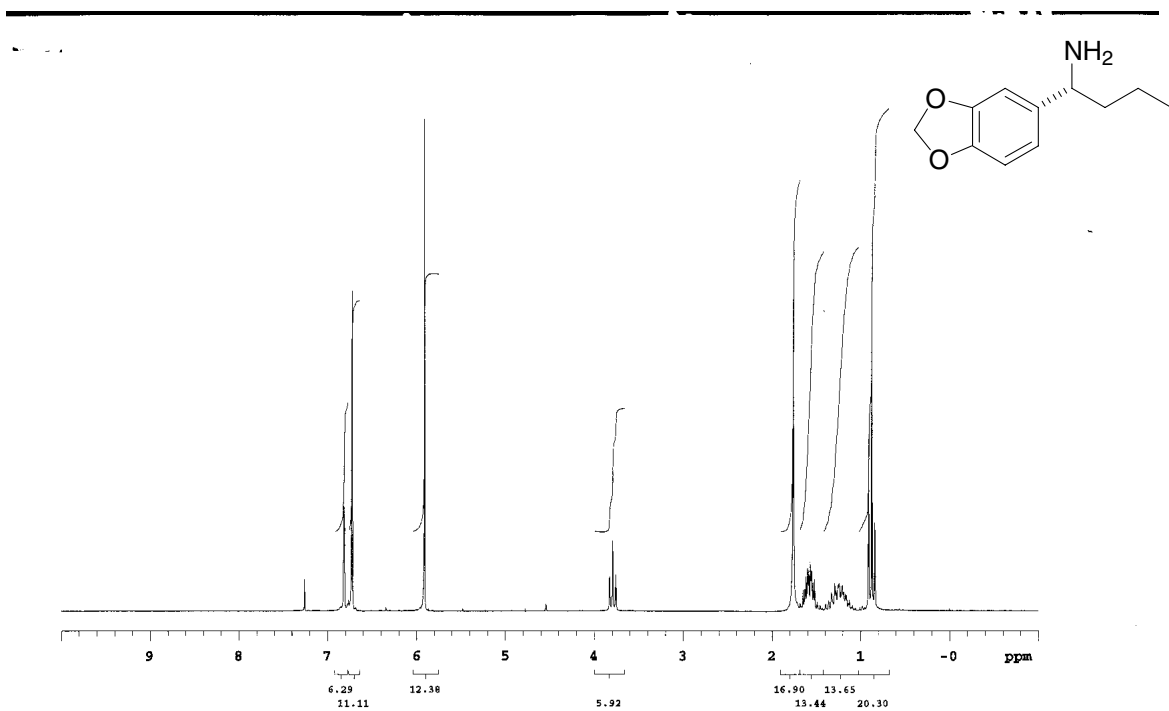
11









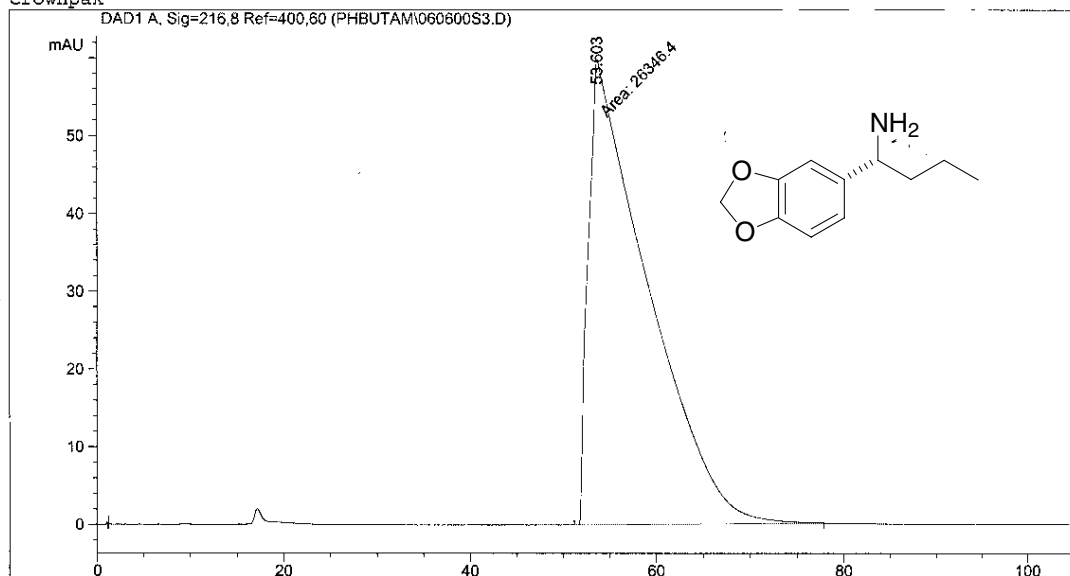


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Injection Date : 6/6/2000 8:40:46 PM      Seq. Line :   3
Sample Name    :                          Vial :   23
Acq. Operator  : Erik van Echten          Inj :    1
                                           Inj Volume : 4 µl

Acq. Method    : C:\HPCHEM\2\METHODS\PHBUTAM.M
Last changed   : 6/6/2000 8:39:12 PM by Erik van Echten
                  (modified after loading)
Analysis Method : C:\HPCHEM\2\METHODS\PHBUTAM.M
Last changed   : 6/7/2000 7:55:17 AM by Erik van Echten
                  (modified after loading)
    
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Crownpak



Area Percent Report

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Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
    
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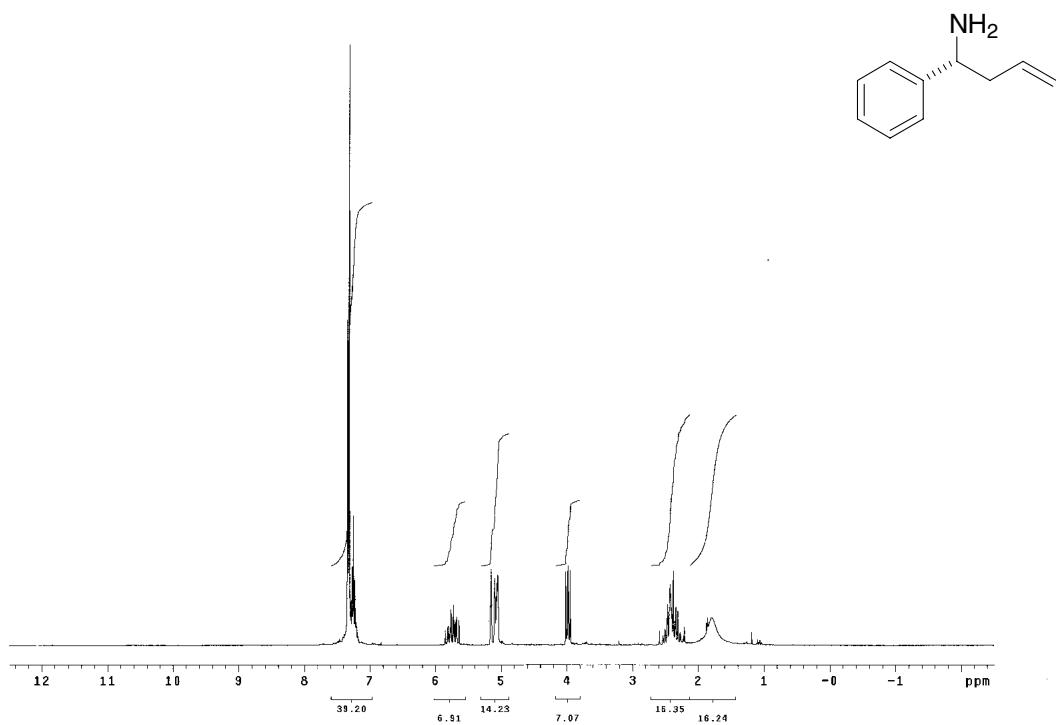
Signal 1: DAD1 A, Sig=216,8 Ref=400,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	53.603	MM	7.3385	2.63464e4	59.83571	100.0000

Totals : 2.63464e4 59.83571

Results obtained with enhanced integrator!

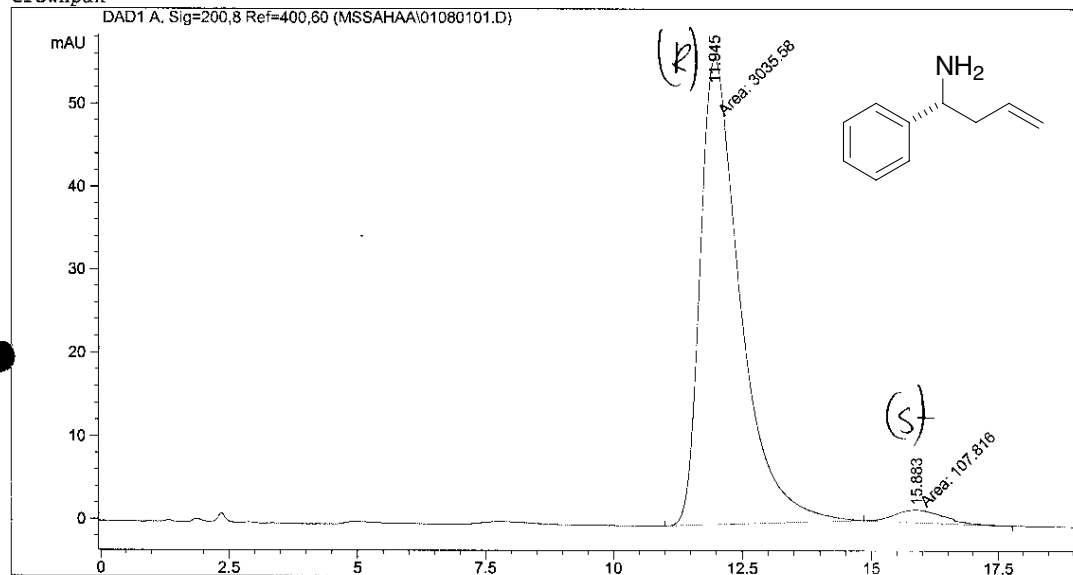
*** End of Report ***



Data File C:\HPCHEM\2\DATA\MSSAHAA\01080101.D

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Injection Date : 8/1/2001 1:43:05 PM
Sample Name : Vial : 11
Acq. Operator : M.Waalderbos/E.v.Echten Inj Volume : 0.5 µl
Method : C:\HPCHEM\2\METHODS\MSSAHAA.M
Last changed : 8/1/2001 1:41:43 PM by M.Waalderbos/E.v.Echten
(modified after loading)

Crownpak



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Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=200,8 Ref=400,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.945	MM	0.9024	3035.57544	56.06339	96.5701
2	15.883	MM	1.1450	107.81596	1.56940	3.4299

Totals : 3143.39140 57.63278

Results obtained with enhanced integrator!

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*** End of Report ***

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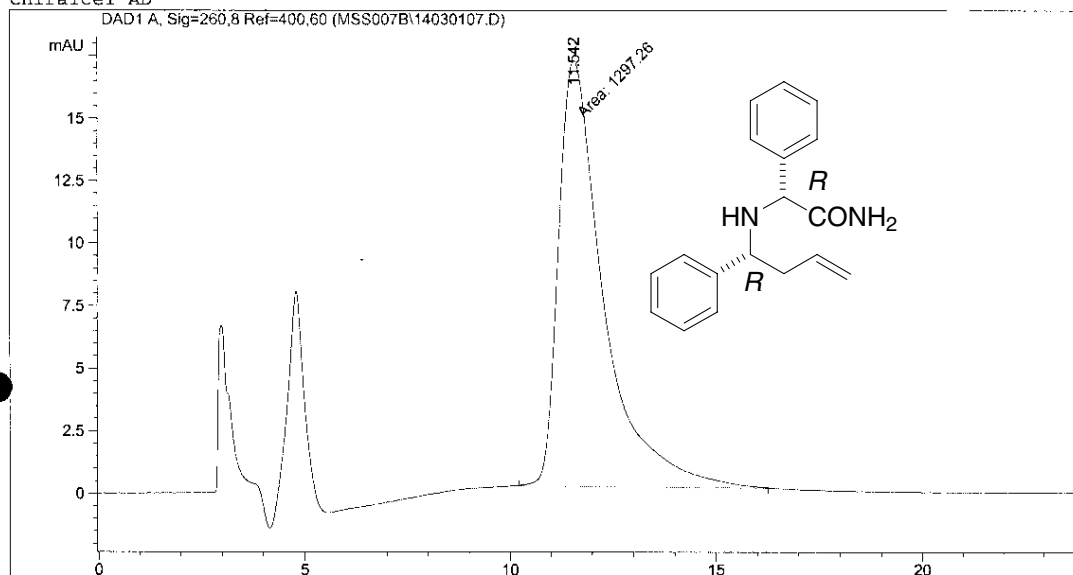
Injection Date : 3/14/2001 5:53:17 PM Vial : 83

Sample Name : Acq. Operator : M.Waalderbos/E.v.Echten Inj Volume : 10 µl

Method : C:\HPCHEM\2\METHODS\MSS007B.M

Last changed : 3/14/2001 5:51:33 PM by M.Waalderbos/E.v.Echten

Chiralcel AD



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Area Percent Report
=====

Sorted By : Signal

Multiplier : 1.0000

Dilution : 1.0000

Signal 1: DAD1 A, Sig=260,8 Ref=400,60

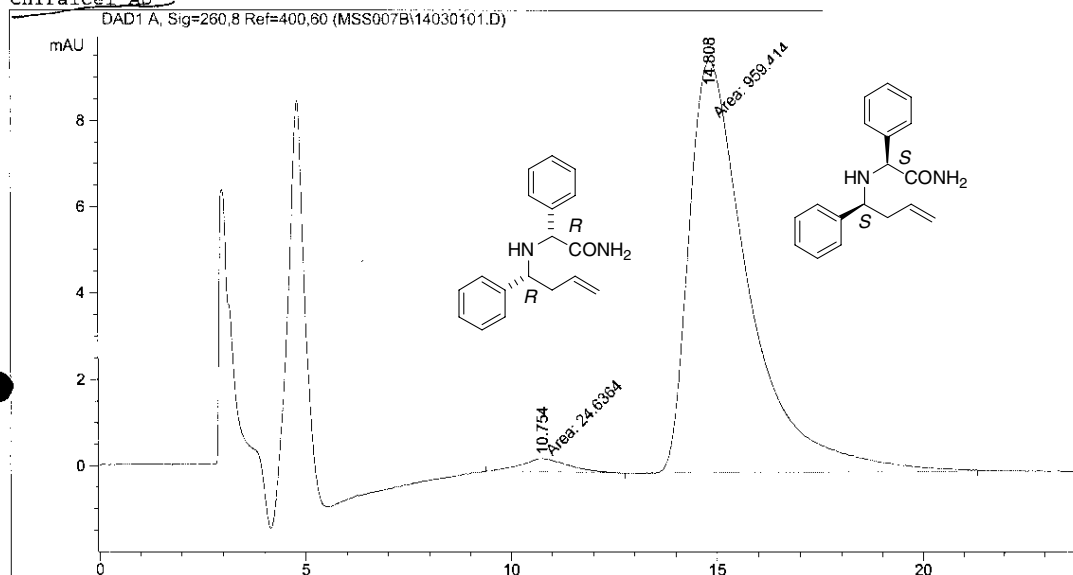
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.542	MM	1.2708	1297.25769	17.01396	100.0000

Totals : 1297.25769 17.01396

Results obtained with enhanced integrator!

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*** End of Report ***

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=====
Injection Date   : 3/14/2001 6:21:53 PM      Seq. Line :    1
Sample Name     :                          Vial       :   84
Acq. Operator   : M.Waalderbos/E.v.Echten    Inj          :    1
                                           Inj Volume  : 10 µl
Method          : C:\HPCHEM\2\METHODS\MSS007B.M
Last changed    : 3/14/2001 5:51:52 PM by M.Waalderbos/E.v.Echten
Chiralcel AD
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Area Percent Report

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=====
Sorted By       : Signal
Multiplier      : 1.0000
Dilution        : 1.0000
=====
```

Signal 1: DAD1 A, Sig=260,8 Ref=400,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.754	MM	1.3234	24.63638	3.10268e-1	2.5036
2	14.808	MM	1.6755	959.41425	9.54345	97.4964

Totals : 984.05062 9.85372

Results obtained with enhanced integrator!

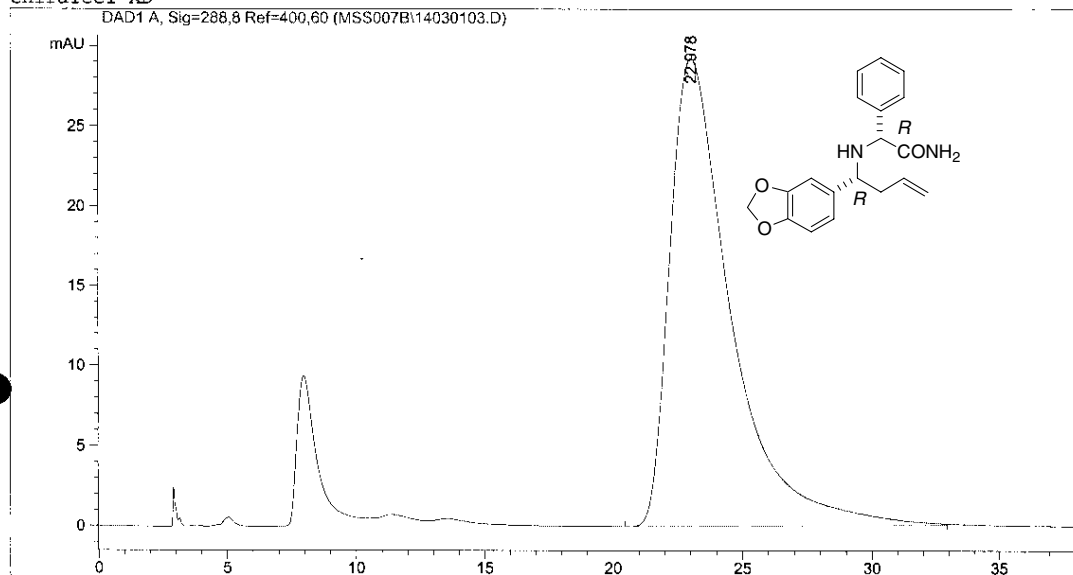
*** End of Report ***

Data File C:\HPCHEM\2\DATA\MSS007B\14030103.D

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Injection Date	: 3/14/2001 7:30:49 PM	Seq. Line	: 3
Sample Name	:	Vial	: 86
Acq. Operator	: M.Waalderbos/E.v.Echten	Inj	: 1
		Inj Volume	: 10 µl
Method	: C:\HPCHEM\2\METHODS\MSS007C.M		
Last changed	: 3/14/2001 5:54:04 PM by M.Waalderbos/E.v.Echten		
Chiralcel AD			

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Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=288,8 Ref=400,60

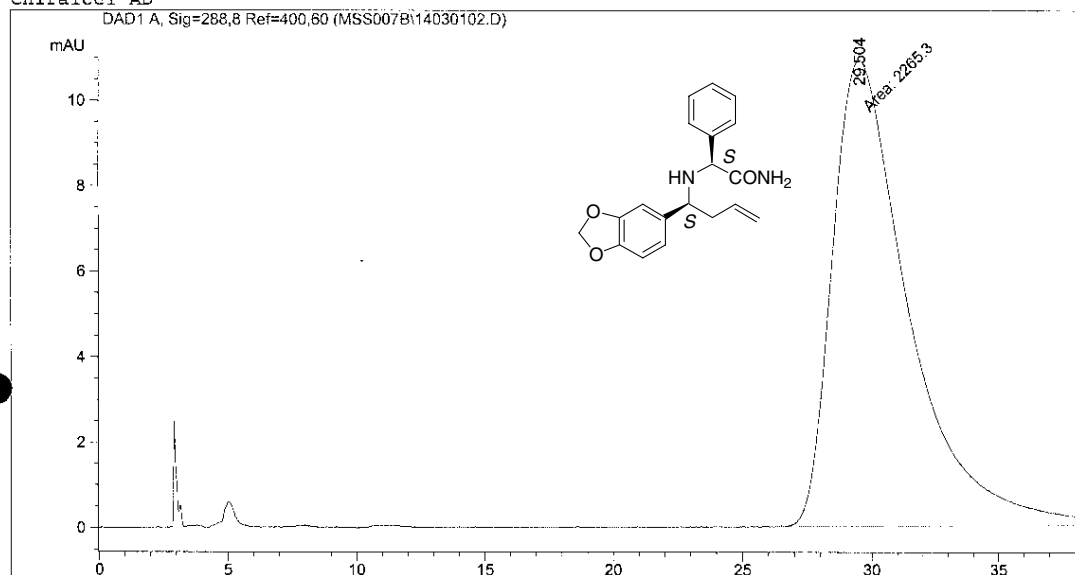
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.978	PB	2.4471	4807.65820	29.22644	100.0000

Totals : 4807.65820 29.22644

Results obtained with enhanced integrator!

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*** End of Report ***

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=====
Injection Date   : 3/14/2001 6:48:50 PM      Seq. Line :    2
Sample Name     :                          Vial       :   85
Acq. Operator   : M.Waalderbos/E.v.Echten    Inj          :    1
                                           Inj Volume  : 10 µl
Method          : C:\HPCHEM\2\METHODS\MSS007C.M
Last changed    : 3/14/2001 5:54:04 PM by M.Waalderbos/E.v.Echten
Chiralcel AD
```



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Area Percent Report
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```
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
```

Signal 1: DAD1 A, Sig=288,8 Ref=400,60

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.504	MM	3.4633	2265.29687	10.90145	100.0000

Totals : 2265.29687 10.90145

Results obtained with enhanced integrator!

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*** End of Report ***